IN THE UNITED STATES PATENT AND TRADEMARKS OFFICE

In the matter of Patent application:

Applicant: Jose A. Ramirez, Navid Omidbakhsh

Assignee: Virox Technologies Inc.

Serial Number: 10/712,990

Filing date: November 17, 2003

Art title: 1616

Title: Hydrogen Peroxide Disinfectant Containing a Cyclic Carboxylic acid and/or Aromatic Alcohol

Examiner: Nathan W. Schlientz, Ph.D; Johann Richter, Ph.D. (Supervisory Patent Examiner)

To: Assistant Commissioner for Patents
The U.S. Department of Commerce,
Patent Office
Washington D.C., U.S.A., 20231

AFFIDAVIT OF NAVID OMIDBAKHSH

I, Navid Omidbakhsh, of the City of Mississauga, in the Regional Municipality of Peel, MAKE OATH AND SAY:

1. I am one of the inventors in respect of this application and the Director of Research & Development of the assignee, Virox Technologies Inc. I have a Bachelor Degree in Chemical Engineering and have almost 10 years of experience in working in the field of chemistry and chemical engineering. Furthermore, I am a Ph.D. candidate at the University of Waterloo, Waterloo, Ontario, and a Member of the Canadian Institute of Chemical Engineers and Canadian Institute of Chemistry. I have reviewed and am familiar with the Final action dated March 27, 2007 and have personal knowledge of the following matters to which I depose.

2. Flexible endoscopes are used in invasive medical procedures and therefore must be disinfected using a disinfectant that has, amongst other things, mycobactericidal and sporicidal activity. They are also heat sensitive and therefore only chemical disinfectants can be used.

3. It is known in the disinfection industry that hydrogen peroxide based solutions are not compatible with flexible endoscopes as they tend to either

damage them and reduce their useful life, or are ineffective in achieving the level of disinfection that is required.

4. The only disinfectants in current use that are not corrosive to flexible endoscopes and which are effective in high level disinfection and sterilization are those containing aldehydes. Aldehydes are toxic and noxious to users and a need exists for alternative formulations that are effective, non-toxic, and which will not damage sensitive medical instruments such as flexible endoscopes.

5. Hydrogen peroxide is non-toxic and user- and environmentally-friendly as the breakdown products are oxygen and water. However, commercial solutions tend to be ineffective in achieving the level of disinfection that is required or are damaging to sensitive medical instruments (e.g. flexible endoscopes).

6. To date, to the best of my knowledge, no company has developed a hydrogen peroxide based disinfectant that has mycobactericidal and sporicidal activity, at short contact times, and that is compatible with flexible endoscopes. Commercial hydrogen peroxide based disinfectants rely on hydrogen peroxide concentrations of 7 w/w % or higher which are damaging to such instruments.

7. Despite the failure of others, I and Jose A. Ramirez, on behalf of Virox Technologies Inc., have succeeded in developing a low-volatility, low toxicity, non-corrosive, non-irritating, and stable aqueous sporicidal and mycobactericidal solution that is compatible with flexible endoscopes. See, for example, page 5, line 23, wherein the present specification states that a "major field of application is in the processing of delicate surgical instruments and devices, including flexible endoscopes." See also page 21, line 16-20 (Example III), wherein Composition II was tested under conditions which simulated conditions present in an endoscope processing machine. See also page 1, line 7 to page 2, line 12 and page 5, line 2-15 of the present specification.

8. As stated in the present specification at page 6, line 28-30, 2-furan carboxylic acid has been described as possessing some bactericidal, fungicidal and mycobactericidal activity, particularly when formulated in combination with traditional mycobactericidal ingredients. The present invention resides in the combination of this compound with hydrogen peroxide in specified concentrations and pH to provide a surprisingly effective mycobactericidal and sporicidal solution that is compatible with sensitive medical devices. See, for example, page 2, line 15-16 of the present specification.

9. The present invention provides solutions which are a dramatic improvement over existing hydrogen peroxide disinfectants. Contact times in high level disinfection may be reduced by factors of up to 4-5 using hydrogen peroxide concentrations which are lower by as much as one order of magnitude compared to prior art solutions (see page 5, line 16-19 of the present specification).

10. The following categories of microorganisms are listed below in terms of difficulty of kill, with bacterial endospores being the most difficult to kill and enveloped viruses the easiest to kill:

    1. bacterial endospores (or simply spores)
    2. mycobacteria
    3. fungi
    4. non-enveloped viruses
    5. bacteria
    6. enveloped viruses

11. Solutions according to the invention containing hydrogen peroxide in a concentration as low as 2 w/w % can be used to inactivate spores and mycobacteria present on sensitive medical instruments, such as flexible endoscopes, without damaging them. We conducted internal tests in which we put flexible endoscopes through 1000 cycles in an endoscope processing machine using a solution according to the present invention and determined that no damage resulted. The solution tested is summarized in TABLE 1 below:

TABLE 1

Raw material	Percent (w/w%)
deionized water	Qs to 100
1-hydroxyethylidene-1,1-diphosphonic acid	0.9
phosphoric acid	1.5
dodecylbenzene sulfonic acid	0.18

C6-diphenyl oxide disulfonate	0.07
2-furan carboxylic acid	1.0
C10-linear alcohol ethoxylate (3.5 moles of ethoxylated, average)	0.05
hydrogen peroxide	2.0
caustic potash	Up to pH=2.5

12. Publication No. WO 99/52360 to Serego Allighieri et al. (Allighieri) and U.S. Patent No. 5,387,605 to Beilfuss et al. (Beilfuss) do not teach or suggest an antimicrobial solution compatible with sensitive medical devices, especially flexible endoscopes. These references also do not teach solutions that have enhanced mycobactericidal and sporicidal activity.

13. Allighieri teaches disinfecting solutions for use on hard surfaces such as those present in a household (e.g. see bottom of page 22 to top of page 23; page 3, second paragraph; page 9, second last paragraph; page 10, last paragraph; and page 11, first two paragraphs). No mycobactericidal or sporicidal activity is suggested or demonstrated.

14. Beilfuss teaches solutions for use in the general disinfection of surfaces, instruments, appliances, skin and hands and contains no specific teaching of disinfection of sensitive medical instruments such as flexible endoscopes (e.g. column 4, line 41-50). While the solutions of Beilfuss are shown to inactivate mycobacteria, longer contact times are required to achieve the same level of disinfection as can be achieved by the present inventive solution. For example, at column 5, EXAMPLE 2 shows that a solution containing 2-furan carboxylic acid in a concentration of 0.5 w/w % takes 30 minutes to inactivate mycobacteria. In contrast, Composition I (containing 0.5 w/w % of 2-furan carboxylic acid and 0.5 w/w % hydrogen peroxide) is effective in inactivating mycobacteria in a contact time of only five minutes. (see page 20, Table 10 of the present application).

15. See also Table II (page 21) of the present application wherein test results show a 0.50 w/w % solution of hydrogen peroxide to be ineffective in killing mycobacteria in a contact time of five minutes and that a 0.50 w/w % solution of 2-furan carboxylic acid is likewise ineffective. However, a combination of hydrogen peroxide and 2-furan carboxylic acid, each present in a concentration of 0.50 w/w % (Composition I), leads to a greater than 5 log reduction in mycobacteria in a contact time of five minutes.

16. Example III of the present application also demonstrates the synergy between H2O2 and 2-furan carboxylic acid, as the other ingredients of Composition II (disclosed at page 11, line 11 onwards) are merely corrosion inhibitors (Cobratec 99, sodium molybdate, sodium nitrite), a buffer (sodium carbonate) and tap water.

17. The present specification contains other examples showing the effectiveness of the present invention in killing a wide range of test organisms, including spores (e.g. *Bacillus subtilis*). Sporicidal activity is demonstrated in Example III (Composition II; page 21, line 16 to page 22, line 10), Example X (Solutions P or Q; page 29, line 3 onwards) and Example XI (Solution R; page 30, line 2 onwards).

18. The synergy between hydrogen peroxide and 2-furan carboxylic acid is quite unexpected. While Beilfuss teaches that hydrogen peroxide may be combined with 2-furan carboxylic acid to increase the spectrum of activity (column 3, line 10-18), there is no teaching that combining these ingredients would lead to an enhancement of disinfecting activity against mycobacteria or spores. Indeed, Beilfuss teaches that the combination of two biocidal ingredients may not lead to any enhancement of activity. For example, see column 6, line 25-30 wherein Beilfuss states, "The example shows that the combination of carboxylic acid according to the invention with other biocidal active ingredients such as benzalkonium chloride is as effective as before against Tb, whilst a combination with acids, for example, phosphoric acid does not develop any efficacy against Tb."

19. To verify that Beilfuss does not teach sporicidal solutions, I tested the solution of Example 3 of Beilfuss for sporicidal activity. The solution tested is summarized below in Table 1.

Table 1: Beilfuss Solution (Example 3)

Ingredient	% w/w (based on total weight of solution)
Deionized water	96.50
Benzalkonium chloride	2.50
Furoic acid	1.00

The Beilfuss Solution was tested using the Quantitative Carrier Test Method I against *Bacillus subtilis* and the results are shown in Table 2 below.

Table 2: The activity of the Beilfuss Solution against *B.subtilis* (QCT 1)

Repeats	Dilution	Contact Temp	Contact Time	Average Log_{10} Red'n
3	Full strength	RT	15 min	less than 0.3
3	Full strength	50°C	15 min	less than 0.3
3	Full strength	RT	6 hours	less than 0.3

RT = room temperature

The results demonstrate that the Beilfuss Solution of Example 3 containing 2.5 w/w % benzalkonium chloride (i.e. 10 pts at 25% dilution) and 1 w/w % 2-furan carboxylic acid (i.e. 2 parts at 50% dilution) does not have sporicidal activity.

20. Given the teachings of Beilfuss and my above experiment, the person skilled in the art would not be able to predict or have a reasonable expectation of success that even a mere additive effect would arise by combining two or more biocidal ingredients. It would therefore not be obvious to the person skilled in the art, reading Beilfuss alone or in combination with Allighieri, that a synergistic mycobactericidal and sporicidal solution, effective at short contact times, would result from a combination of 2-furan carboxylic acid with another active ingredient (e.g. hydrogen peroxide).

21. For these reasons, I believe the claimed invention is not obvious in light of Allighieri and Beilfuss.

Sworn before me in the City of Toronto,)
Province of Ontario, DK .)
This 18th day of ~~June~~ July, 2007)
)
)

Navid OMIDBAKHSH

Dolly Kao, Commissioner for Taking Oaths